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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,589	HALBLEIB ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/22/2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-25, 29* is/are rejected.

7)☒ Claim(s) *26-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09222004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 16-29 are pending and under consideration.

Response to Amendment

The objection to the Title has been obviated by Applicant's amendment and is thus withdrawn.

The rejections over claims 1-15 have been rendered moot by cancellation of the claims and are thus withdrawn.

New issues are set forth below.

Claim Objections

Claims 26-28 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. The specification as originally filed does not provide support for the invention as now claimed: The method of claim 22 wherein high affinity is characterized by a Kd of 0.7 to 2.5 nM.

Applicant's amendment, filed 9/22/2004, does not provide sufficient direction for the written description for the limitation of claim 23 wherein in the high affinity is characterized by a Kd of 0.7 to 2.5 nM. The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide direction for the instant sequence encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.

Claim 20, 29 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of monitoring binding reactions between fluorescently labeled ligands in the presence of test compounds, and measuring the results by measuring fluorescent polarization, wherein the fluorescently labeled ligands are dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten, does not reasonably provide enablement for methods of monitoring

binding reactions between fluorescently labeled ligands in the presence of test compounds, and measuring the results by measuring fluorescent polarization, wherein the fluorescently labeled ligands are derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 20, 29 are overly broad since insufficient guidance is provided as to which derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten will function in the claimed method. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten. Since the claims encompass derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a functional limitation for the derivatives encompassed by the claims. Since detailed information regarding the structural and functional requirements of the derivatives are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Since the claims do not enable one of skill in the art to practice the claimed method using derivatives, and since detailed information regarding the structural and functional requirements of the derivatives are lacking, it is unpredictable as to which derivatives, if any, meet the limitations of the claims.

Claims 20, 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in paper NO. 10, 9/26, 2002. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to methods of monitoring binding reactions between fluorescently labeled ligands in the presence of test compounds, and measuring the results by measuring fluorescent polarization, wherein the fluorescently labeled ligands are derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten. The specification and claim do not place any limit on the derivatives of dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, dexamethasone, 4-pregnen, 5a-androstan, and 4-androsten are insufficient to describe the genus. One of skill in the

art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the term "high affinity ", which is a conditional term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific parameters supported by the specification which Applicant considers to be "high affinity".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-22, 24-25, are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/27365 (Lustig et al.) in view of U.S. Patent No. 6,248,520 (Roeder et al.), and further in view of in view of U.S. Patent No. 6,054,295.

The claims are drawn to methods of monitoring binding reactions between fluorescently labeled ligands and nuclear hormone receptor in the presence of test compounds, and measuring the results by measuring fluorescent polarization. The claims are not patentable because the Lustig et al. reference teaches a method of screening for modulators of nuclear hormone receptor function comprising measuring the binding of a sensor polypeptide at sub-micromolar concentrations to a nuclear hormone receptor in the presence of a candidate agent, and comparing the result to a control (Lustig at 2). The sensor comprises a peptide with a receptor binding sequence and a fluorescent label, and the measurement is by fluorescent polarization assay (Lustig at 5). The Lustig reference further teaches that the fluorescent label may be fluorescein, and may be coupled to the sensor polypeptide via a linker (Lustig at 7). The reference further teaches that the receptor may comprise only a portion of a full-length receptor, specifically the ligand-binding domain (Lustig at 3). The reference further teaches that the sensor is present at less than 1 nM (Lustig at 7).

The Lustig reference differs from the claims in that it does not teach the method wherein the receptor is GR, AR or PR, or wherein the LBD is bound to GST. However, the '520 patent

discloses methods of screening for compounds which act as antagonists for steroid hormones where in the hormone receptor is androgen receptor (AR) glucocorticoid receptor (GR) or progesterone receptor (PR) ('520 at column 12, line 55 to column 13, line 5). Additionally, the '295 patent discloses fusion constructs expressing both full length nuclear receptors fused to GST coding sequences, as well as ligand binding domains of nuclear hormone receptors fused to GST ('295 at column 14 ,lines 5-20). Therefore it would have been obvious to one of skill in the art at the time the invention was made to practice a method of screening for modulators of nuclear hormone receptor function comprising measuring the binding of a sensor polypeptide at sub-micromolar concentrations to a nuclear hormone receptor in the presence of a candidate agent, and comparing the result to a control by measuring the fluorescence polarization of the solution of the solution and comparing the fluorescence polarization of the solution in the presence and absence of the compound to indicate any competitive interaction, wherein the receptor is GR, AR or PR, or wherein the LBD is bound to GST. The motivation and expectation of success are provided in the '520 patent which discloses that there is a need for pharmaceutical compositions that can modulate the activation of nuclear hormone receptors, since nuclear hormone receptors play a vital role in mediating gene expression, cell growth and differentiation, development of an organism, and homeostasis, such modulation provides a valuable tool for treating numerous cancers, which involve uncontrolled differentiation, particularly in tissues comprising the sexual and reproductive organs, and in brain, muscle or adipocyte tissue '520 at column 2, line 64 to column 3, line 5). Additional motivation is provided by the '295 patent which disclose that the fusion proteins are useful in assays to

identify compounds which modulate wild type nuclear hormone receptors ('295 at column 14, lines 5-10).

Conclusion

Claims 16-25, 29 are rejected.

Claims 26-28 are objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

References

The Office will no longer be supplying paper copies of U.S. Patents cited in Office Actions. Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office

of Public Records and from commercial sources. Applicant may direct inquiries about the use of the Office's PAIR system to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1646
November 22, 2004

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PATENT EXAMINER